IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Patent Application of:
Alastair Hodges et al.

Application No.: 10/624,795

Filed: July 22, 2003

For: ELECTROCHEMICAL CELL

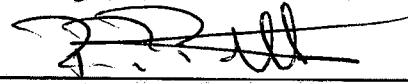Confirmation No.: 7470

Art Unit: 1753

Examiner: A.S. Noguerola

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§ 1.132 Declaration of Alastair Hodges

I, Alastair Hodges, residing at 15 Jasmine Court, Blackburn South, Victoria, Australia, hereby declare as follows:

1.   I am Chief Scientist for Universal Biosensors Pty Ltd, where I work as head of the Research and Development Department and my responsibilities include, but are not limited to, supervision and direction of all of the company's technical endeavors, analysis of the output of the research projects and future direction setting of the same, management of the Research and Development Department, and management of the company's intellectual property. I have been employed at Universal Biosensors in this capacity since the founding of the company over seven years ago. During the earlier years of the development of the company, I also served as General Manager of Universal Biosensors. Prior to my employment at Universal Biosensors, I worked as a research scientist in the Defence Science and Technology Organisation and the Australian Commonwealth Scientific and Research Organisation for approximately eight (8) years, where I

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worked in the fields of electrochemistry and transport processes, and at Memtec Limited and its successors for approximately seven (7) years, where I worked on sensor technologies. Between 1999 and 2001, I was in charge of a team that worked in the United States on the development of glucose sensor technology. I have been working specifically in the field of electrochemical sensors for more than fourteen (14) years and in the general field of electrochemistry for more than twenty-seven (27) years. I have at least thirteen (13) papers published in refereed journals. Furthermore, I am the primary inventor of national and international patents in at least thirty (30) different patent families, and have national and international patent applications pending in at least an additional ten (10) patent families.

2.   I obtained a Bachelor of Science in Chemistry with Honors from the University of Melbourne in 1980. I obtained a PhD in electrochemistry from the University of Melbourne in 1987.

3.   I have read the above-referenced application and I fully understand the materials disclosed and claimed therein.

4.   The above-referenced patent application is directed to apparatuses for determining a concentration of glucose in a blood sample.

5.   The present invention is an improvement over previous apparatuses for determining a concentration of glucose in a blood sample because the particular design results in improved accuracy, reliability, and/or speed in comparison to previous apparatuses. More particularly, these improvements are a direct result of the electrode configuration of a hollow electrochemical cell of the apparatus (facing each other, located on different planes, and separated by a distance of from about 20 microns to about 200 microns), the walls of a spacer of the cell and the electrodes defining the hollow cell, a fluid permeable side-wall on at least one side of the hollow cell, the effective cell volume of the hollow cell (less than 1.5 microliters), and the circuitry that is configured to apply an electric potential difference between the electrodes, measure a current between the electrodes, and determine both the diffusion coefficient and the concentration of a redox mediator in the cell from cell current. The recited electrochemical apparatus achieves a steady-state current. As a result, the invention *can independently determine* the diffusion coefficient *and* the concentration of the redox mediator by comparing a measure of the steady-state current with the rate at which the current varies in the current transient before the steady-state is achieved. (*See* para. [0056] of the published

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application.)

6.   An apparatus for determining a concentration of glucose in a blood sample that relies on the Cottrell equation *cannot* independently determine both the diffusion coefficient and the concentration of a redox mediator in an electrochemical cell from cell current. This is because an apparatus that relies on the Cottrell equation *cannot* achieve a steady-state current. In a Cottrell system, the electrochemical species near the electrode of the system is depleted. The system generates a current versus time plot that subsequently follows the Cottrell equation. A Cottrell current is defined by the equation:

$$i = \frac{nFA\sqrt{D}C_0}{\sqrt{\pi t}}$$

where:

- i is the current measured;
- n is the number of moles of electrons transferred per mole of electroactive species reacted;
- F is Faraday's Constant;
- A is the electrode area;
- D is the diffusion coefficient of the electroactive species;
- C_0 is the concentration of the electroactive species; and
- t is time.

(*See* col. 1, line 67 to col. 2, line 14 of U.S. Patent No. 5,243,516 of White.) Current and time are inversely proportional such that as time continues to lapse, the current continues to dissipate. Accordingly, it is mathematically impossible for a Cottrell current to achieve steady-state.

7.   The claimed embodiment requires circuitry for an independent determination of the concentration and the diffusion coefficient of the redox mediator. As a person having ordinary skill in the art would understand, such an embodiment cannot analyze a Cottrell current and achieve accurate results. Further, it is also impossible to independently determine both a diffusion coefficient of an electroactive species (D) and a concentration of the same electroactive species (C_0) from a Cottrell current because the two values are mathematically dependent on each other. Thus, even if all of the other variables (the current (i) at various intervals of time (t), the number of moles of electrons transferred per mole of mediator reacted (n), the area of the working electrode (A), and Faraday's constant (F)) are known, it is only possible to determine the product concentration times

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the square root of the diffusion coefficient ($C_o\sqrt{D}$). Accordingly, it is not possible to determine the concentration of the electroactive species *independent* of the diffusion coefficient of the electroactive species for a device that relies on Cottrell current. (*See* para. [0056] of the published application.) As discovered by the inventors, such a determination can be made, however, by comparing *the measured steady-state current* and the current transient before the steady-state is achieved. (*Id.*) The Examiner's suggested combinations, at best, only rely on estimates and extrapolations of a steady-state current; the combinations do not *measure* a steady-state current because a steady-state current *cannot* be achieved by Diebold and White. Further, the Examiner's reference to paragraph [0075] of the present application, which states that an early part of the current vs. time curve can be analyzed by the Cottrell equation, is inappropriate. This paragraph of the application merely illustrates an alternate embodiment of an apparatus for determining a concentration of glucose in a blood sample and is not the claimed embodiment, which requires the circuitry for making the two recited independent determinations.

8. U.S. Patent No. 5,243,516 of White ("White") is directed to a biosensing instrument that uses Cottrell current in order to make measurements with respect to current and time. (*See at least* col. 2, lines 62-64.) More specifically, the teachings of White are aimed at making biosensing instruments that use the Cottrell equation more accurate by recognizing non-Cottrell behavior and classifying results from non-Cottrell behavior as *invalid*. (*See at least* col. 2, lines 35-59, col. 7, lines 38-47, and claims 1-8, i.e., every claim of White; emphasis added.) White clearly teaches what one of ordinary skill in the art knew at the time and knows today – that non-Cottrell behavior negatively impacts the accuracy of a meter that uses the Cottrell equation to make measurements. Further, the teachings of White, which focus on *eliminating* non-Cottrell behavior, would not be combined with teachings that use Cottrell behavior. Such a combination completely contradicts the purpose of White.

9. Diebold teaches using a meter like that of White to make measurements using the electrochemical sensor of Diebold. (*See* col. 13, lines 9-26.) Thus, because the meter of White is focused on *eliminating* results tied to non-Cottrell behavior and only relying on results tied to Cottrell behavior, it is clear that Diebold also relies on the Cottrell equation. More specifically, Diebold is clearly *not* designed to achieve a steady-state current because devices that rely on Cottrell *cannot* achieve a steady-state current. If non-Cottrell behavior was incorporated into the device of Diebold

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and White as the Examiner proposes, the results would all be classified as *invalid* in accordance with the specific teachings of White.

10.   While paragraph [0056] of the present application discusses the fact that a thin layer cell eventually achieves a steady-state concentration profile if both oxidized and reduced forms of a redox couple are present, such a configuration results in current that has non-Cottrell behavior (i.e., it cannot be represented by the Cottrell equation). It is mathematically impossible for a steady-state current to be achieved for a Cottrell current. It is clear from the teachings of Diebold, in particular because of its reliance on White, that the sensor of Diebold is unlike the present application, at least because it utilizes a Cottrell current and does not achieve a steady-state current. Further support of the failure to achieve a steady-state current was previously illustrated by extracting data from Figure 3 of White. While the Examiner has requested a similar plot for ten seconds worth of data points, such an extrapolation would conceivably be ripe with errors. Instead, a person having ordinary skill in the art would understand the behavior of the White meter by looking to the source of the behavior – the equation by which the behavior is governed. Thus, looking to the Cottrell equation, it is observed that a steady-state current is impossible to achieve. While the change in current certainly decreases as time elapses, the change is never zero. Even if the change is considered negligible after an extended period of time, that still does not provide the data necessary in order to make an independent determination of both the diffusion coefficient and concentration. As discovered in our work, only by comparing a measure of the steady-state current with the rate at which the current varies in the current transient before the steady-state is achieved were we able to make these independent determinations. None of the references cited by the Examiner teach such a discovery.

11.   It is also worth noting that the electrodes of Diebold are planar electrodes. (*See at least* col. 4, line 23 to col. 5, line 5 and col. 8, lines 17-29.) A planar electrode does not refer to the shape of the electrode, but rather, the geometry of diffusion volume surrounding the electrode and its resulting electrochemical behavior. The electrode in Diebold is planar because the electroactive species diffuses to the electrode from an essentially flat planar volume. (*See* col. 12, line 68 to col. 13, line 8.) This is different than a microdisk electrode, for example, in which the electroactive species diffuses to the electrode from a hemispherical volume. An electrode cannot be both a planar electrode and a microdisk electrode because the electrode cannot have two different diffusion volumes surrounding the electrode. The fact that microdisk electrodes *cannot* be planar electrodes is

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relevant because some of the teachings the Examiner relies upon requires microdisk and/or microsphere electrodes and it is the specific characteristics of each of the electrodes that allows it to operate in the manner it does. Such electrodes are not easily interchangeable. A simple substitution of one type of electrode for another cannot achieve the Examiner's desired results.

12.   The recited apparatus for determining a concentration of glucose in a blood sample includes both a hollow electrochemical cell *and* circuitry that is configured to determine both the diffusion coefficient of a redox mediator in the electrochemical cell and independently its concentration from cell current. Neither Diebold nor White discloses a device or method teaching such circuitry. This is at least because both references rely upon the Cottrell equation to make measurements, which inherently cannot allow for such an independent determination. (*See* para. [0056] of the published application.) The Examiner proposes two separate circuitry options to be used in combination with the electrochemical sensor of Diebold and the meter of White to arrive at the recited invention. One circuitry option stems from an article authored by Guy Denuault et al. entitled "Direct determination of diffusion coefficients by chronoamperometry at microdisk electrodes" ("Denuault"). The second circuitry option stems from an article authored by László Daruházi et al. entitled "Cyclic voltammetry for reversible redox-electrode reactions in thin-layer cells with closely separated working and auxiliary electrodes of the same size" ("Daruházi").

13.   Neither Denuault nor Daruházi is compatible with Diebold and White because Denuault and Daruházi rely on *non*-Cottrell behavior. Thus, because White is specifically designed to *invalidate* results from non-Cottrell behavior, the results created by the teachings of either Denuault or Daruházi would be invalidated in the configuration proposed by the Examiner. Unlike a Cottrell system (a system in which behavior follows the Cottrell equation), in which the electrochemical species near the electrode is depleted evenly for a planar volume, in non-Cottrell systems like that of Denuault and Daruházi, the electroactive species near the electrode is either not fully depleted or is depleted more quickly or more slowly at an edge of the electrode than at the center of the electrode. The resulting current versus time plot in a non-Cottrell system is, by definition, non-Cottrell in nature – i.e., the current *can* achieve a steady-state. Further, even if the results from either Denuault or Daruházi can include Cottrell behavior, as the Examiner suggests at least with respect to page 30 (top) and page 31 (bottom) of Denuault, an independent determination of *both* the diffusion coefficient and the concentration of the redox mediator *cannot* be determined

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from the Cottrell behavior. This is because these two parameters are dependent on each other in the Cottrell equation.

14.   The teachings of Denuault are directed to microdisk and microsphere electrodes. Both microdisk and microsphere electrodes are not *planar* electrodes. Furthermore, both microdisk and microsphere electrodes have non-Cottrell behavior. While a person having ordinary skill in the art would recognize that microdisk and microsphere electrodes are not planar electrodes (the type used in Diebold), Denuault makes it clear that microdisk electrodes and planar electrodes are two different types of electrodes by listing a planar electrode, a rotating disk electrode (RDE), and a microdisk electrode as types of electrodes that have different sizes and geometries at page 28, paragraph 2. The diffusion volume surrounding a planar electrode is a flat planar volume; the diffusion volume surrounding a microdisk electrode is a hemispherical volume and a spherical volume for a microsphere electrode (*See* p. 29, para. 3 of Denuault; *see also* para. 11 herein.) This is important because it is the shape of the diffusion volume surrounding an electrode that helps determine how the current will behave.

15.   Microdisk electrodes of Denuault have edge effects that allow for a diffusion coefficient to be calculated. Planar electrodes do not produce similar edge effects, and thus the methods relied upon to teach calculating the diffusion coefficient for microdisk electrodes cannot be relied upon to teach calculating the diffusion coefficient for planar electrodes. This is independently confirmed in an article from the Bulletin of the Korean Chemical Society entitled "Simultaneous determination of Diffusion Coefficient and Concentration by Chronoamperometry at a Microdisk Electrode" by Jung et al. ("Jung"). Jung specifically teaches that the disclosed analysis methods for calculating a diffusion coefficient are only applicable for microdisk electrodes and specifically states that its methods *are not compatible with planar electrodes*. (*See* beginning of first full paragraph of first column of page 210 to fourth full paragraph of first column of page 211 of Jung, which is attached for the Examiner's convenience; emphasis added.) Similarly, the techniques taught by Denuault for calculating diffusion coefficients and concentrations for microdisk and microsphere electrodes cannot be applied to planar electrodes like those of Diebold.

16.   The measure of current at any time for a microdisk electrode is described in Denuault by Equation 3: $i_d(t) = \pi^{1/2} n F D^{1/2} c^* a^2 t^{-1/2} + 4nFDc^* a$. As time approaches infinity, the first term

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becomes negligible and the measure of current as time approaches infinity is approximately $4nFDc^*a$. This result is the same as Equation 1 of Denuault. Equation 1 indicates that the steady-state tip current of a scanning electrochemical microscope (SECM) is $4nFDc^*a$. A tip current of a SECM acts like current of a microdisk electrode, which is why as t approaches infinity, the current for each behaves similarly. Unlike electrodes that rely on a Cottrell current, a steady-state current *can* be achieved with a microdisk electrode. In neither a microdisk electrode nor the SECM, however, is the achieved steady-state current zero at infinite time. This is because the value of the steady-state current is defined by the geometry of the diffusion. This was discussed with the Examiner in particular with respect to Jung. (*See* beginning of third full paragraph of first column of page 210 of Jung.) For a planar electrode where the current follows the Cottrell equation, on the other hand, at infinite time there is no current flowing and thus it cannot be characterized as a steady-state *current*. (*Id.*)

17. In the Advisory Action dated May 11, 2009, the Examiner states that Equations 1 and 2 of Denuault appear to be hypothetical constructs because they are not equal. A person having ordinary skill in the art, however, would not expect these two equations to be equal because they represent current values for different diffusion geometries. Equation 1 is for the tip current of a SECM, while Equation 2 is for the current of a microsphere electrode. As discussed above in paragraph 14, one would expect the tip current of a SECM to more closely resemble the current of a microdisk electrode, which indeed it does. As t approaches infinity, the value for the current for both a SECM and a microdisk electrode is $4nFDc^*a$. As indicated by Equation 2,

$$i_s(t) = \frac{nFAD^{1/2}c^*}{\pi^{1/2}t^{1/2}} + \frac{nFADc^*}{r_s},$$ on the other hand, as the current approaches infinite time, the first

term becomes negligible and the measure of current as time approaches infinity for a microsphere electrode is approximately $\dfrac{nFADc^*}{r_s}$. These values for the current of the SECM and microdisk electrode as t approaches infinity and for the current of the microsphere electrode as t approaches infinity are *different* because of the *different diffusion volumes involved*. They are not hypothetical constructs. Thus, contrary to the Examiner's statements, Equations 1-3 provide *further support* for the fact that it is the geometry of the diffusion volume that affects the behavior of the current. What determines whether or not the diffusion geometry is planar or hemispherical is not necessarily the

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shape of the electrode, but rather, it is the relative contribution of material diffusing from liquid surrounding the edges of the electrode to material diffusing from liquid surrounding the rest of the electrode away from the edges. If the area of the electrode is large compared to the area close to its edges, or, alternatively, the electrode edges are masked so they are not surrounded by liquid at all, then there will be essentially planar diffusion. If the area of the electrode is small compared to its edges, such as in a microdisk electrode, then it will have essentially hemispherical diffusion.

18.   Further, the second terms of Equations 2 and 3 of Denuault, which do not include a time component, are not merely correction factors as argued by the Examiner in the final Office Action dated January 5, 2009. Rather, the equations are a direct result of the geometry of the diffusion associated with each respective electrode, which in turn allows them to be non-Cottrell in nature. The second factor of each of the two equations is what allows a steady-state current to be calculated. The second factor is representative of the diffusion volume that results from the electrode. Thus, because Equations 2 and 3 are related to microdisk and microsphere electrodes, respectively, the second factor of Equations 2 and 3 include the radii of the electrodes. In fact, each of the current calculations disclosed by Denuault includes a radius. (*See* THEORY section on page 29, illustrating calculations used to determine the diffusion coefficient D, which is a function of the radius a of the microdisk; Equations 10-13; the last paragraph on page 31; and page 32, including Equation 14.) The Cottrell equation, on the other hand, does not contain a second factor. To the extent that an electrode that has a radius behaves in a Cottrell manner, the only effect the radius has on the current is that it helps to define the electrode area A. The radius of an electrode that behaves in a Cottrell manner has no further effect on the current measured. Planar electrodes like those of Diebold, if they happened to be round, do not have a radius that contributes to the current flowing other than by determining the electrode area, and thus cannot be used in the methods of Denuault.

19.   Denuault fails to provide a single teaching that does not rely on the value of the radius of a microdisk or microsphere electrode because the radius helps achieve the desired steady-state current to make the desired determinations. These non-Cottrell behaviors are incompatible with the teachings of Diebold and White. The Denuault equation requires a steady-state to be achieved, but no steady-state current can be achieved with a Cottrell current response like those of Diebold and/or White.

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20.   The teachings of Daruházi are directed to a slow potential sweep process that is used to determine a diffusion coefficient of a substrate and a distance between working and auxiliary electrodes. Daruházi relies on achieving a steady-state current in order to perform its desired calculations. (*See at least* p. 78, para. 2, explaining that the determinations made by its cell are the result of an enhanced current response and a steady-state current; p. 79, the paragraph under Equation 3, stating that it is assumed that t_r is long enough *to reach the steady-state*; emphasis added; p. 81, Equation 32, illustrating that the value of the steady-state current, I_{ss}, is based, in part, on the values of the diffusion coefficient, D, the concentration of glucose, c^o, and the distance between the electrodes,δ; and p. 87, paras. 4-5, indicating that the determination of a ratio comparing the diffusion coefficient, D, and the distance between the electrodes, δ, is based on achieving stable steady-state current values.) Slow potential sweeps are performed, which in turn allows *a ratio δ/D to be determined from Equation 32*. (*See* p. 87, para. 4; emphasis added.) Equation 32, found on page 81 of Daruházi, indicates that a steady-state current value is based, in part, on the values of the diffusion coefficient (D), the concentration of glucose (c^o), and the distance between the electrodes (δ):

$$I_{ss} = \frac{nFADc^o}{\delta}$$

where:

- I_{ss} is the steady-state current measured;
- n is the number of moles of electrons transferred per mole of electroactive species reacted;
- F is Faraday's Constant;
- A is the electrode area;
- D is the diffusion coefficient of the electroactive species;
- c^o is the concentration of the electroactive species; and
- δ is the distance between the working electrode and the auxiliary electrode.

21.   Equation 32 of Daruházi *is not* dependent on time because it relies on *achieving a steady-state*. Thus, because a steady-state current is achieved, the current associated with Daruházi *cannot* be a Cottrell current, and accordingly, cannot be compatible with devices and methods that rely on Cottrell current (e.g., the devices and methods disclosed in Diebold and White). Such a combination would not work, and in fact, in view of the teachings of White, each of the results from Daruházi would be omitted as being an error because the results are non-Cottrell.

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22.   Although the present invention, Diebold, and Daruházi each disclose thin layer electrochemical cells, it is not contradictory that only the present invention and Daruházi rely on non-Cottrell behavior while Diebold relies on Cottrell behavior. As discovered by the inventors, the present invention is operative, at least in part, because it requires a particular spacing between the working and counter electrodes so that a steady-state current can be achieved within the time of a practical test. (*See at least* paras. [0050] and [0056] of the published application.) If the distance between the working and counter electrodes is greater than the upper limit of this range, then for all practical applications the electrode will behave like a planar electrode and it will have a Cottrell current response. The present application discloses that a steady-state current can be achieved with working and counter electrodes spread apart up to approximately 500 microns, and thus the recited upper limit of about 200 microns is well within the disclosed range. (*Id.*) Diebold, on the other hand, fails to disclose a distance between its working and counter electrodes. Nevertheless, because the electrochemical sensor of Diebold is combined with the meter of White, and further because the meter of White seeks to *avoid* non-Cottrell behavior, clearly the spacing between the electrodes of Diebold must be such that Cottrell behavior results. Thus, the spacing can be inferred to be greater than 500 microns. As for Daruházi, like the present application it relies upon achieving a steady-state current. While Daruházi does not disclose a distance between its working and counter electrodes (it teaches solving for this value), two examples provided in Daruházi include a spacing between the electrodes that is equal to 82 ± 10 microns and 72 ± 10 microns. (*See* p. 87, para. 5.) However, spacing between the working and counter electrodes of Diebold, in view of these examples of Daruházi, would never have been equal to 82 ± 10 microns or 72 ± 10 microns, or even less than 500 microns for that matter, because doing so would have contradicted the Cottrell-based teachings of Diebold. Accordingly, a "thin" electrochemical cell can rely on either a Cottrell current or a non-Cottrell current, depending at least in part on the actual spacing between the electrodes.

23.   Even if the teachings of Daruházi could be combined with the teachings of Diebold and White to arrive at the present invention, the methods taught by Daruházi are not desirable for use in an apparatus of the type of Diebold and White. A glucose meter like that of Diebold and White is designed to act quickly to provide a fast determination of the concentration of glucose in a sample of blood. Daruházi, on the other hand, relies on cyclic voltammetry to make its measurement determinations. (*See at least* ABSTRACT on p. 77.) In particular, a slow potential sweep is performed in order to determine the ratio of δ/D. (*See* p. 87, para. 4.) The amount of time it would

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take to perform such a sweep would likely be much greater than the time it would take to perform the methods of White in conjunction with the cell of Diebold. Accordingly, the length of time it would take to perform such a sweep would be prohibitive. More particularly, Daruházi requires a series of experiments in order to make its determination, while Diebold and White only require a single experiment. (*See* p. 87, para. 3 of Daruházi.) Diebold indicates that the time to conduct an experiment is about 10 seconds, while White indicates that the time to conduct an experiment is between 10 and 30 seconds. (*See at least* col. 13, lines 4-6 and Figure 9 of Diebold and col. 5, lines 44-48, col. 6, lines 19-20, and Figure 3 of White.) Daruházi, on the other hand, requires approximately at least 260 seconds. Based on the information provided on page 87 and in Figure 6, the series of experiments taught by Daruházi would result in the following process:

a. Performing a slow potential sweep between −0.2 V and +0.9 V at 5 mV/s; this would take approximately 240 seconds;

b. Performing a reverse sweep in order to bring the system back to a desired starting configuration, or allowing the system to relax with the voltage disconnected (for purposes of this calculation, no additional time is added, although certainly this step would require some amount of time to elapse); and

c. Performing a second potential sweep between −0.2 V and +0.9 V, but at 50 mV/s; this would take approximately 24 seconds.

Thus, just based on the two sweeps provided for in Daruházi, *without* accounting for the time required to reset the system in between the two sweeps, approximately at least 264 seconds (i.e., nearly four and one-half minutes) elapse when performing the methods disclosed by Daruházi. This length of time is incompatible with glucose sensor tests in devices like those disclosed by Diebold and White.

24. Not only is the length of time as a result of the potential sweep taught by Daruházi not desirable, but the electronics required to perform a potential sweep like the sweep of Daruházi are significantly different than the types of electronics taught by Diebold and White. Incorporating electronics related to performing a potential sweep into the devices and methods of Diebold and White would be both difficult and undesirable. In accordance with the teachings of Daruházi, external electronic circuitry is required to sweep the voltage of the working electrode up and/or down. The response of the current is measured as a function of the voltage of the working electrode. Thus, in order to employ this technique, the potential or voltage of the working electrode must be

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known and must be able to be controlled externally.

25.   As taught by Daruházi, one way of knowing and externally controlling the potential or voltage of the working electrode is to use three electrodes. (*See at least* para. 1 of Theory section on p. 78 and para. 1 of Experimental section on p. 83.) The three electrodes (a working electrode, a counter or auxiliary electrode, and a reference electrode) are connected such that there is a very high impedance in the circuit between the working and reference electrode and a relatively low impedance between the working and the counter or auxiliary electrode. The electronics of the circuit apply a voltage between the working and auxiliary or counter electrodes that causes a current to flow therebetween, and the voltage applied is adjusted by the electronics so that the voltage difference between the working and reference electrodes is kept at a desired level or series of levels (e.g., swept). Based on the known potential of the reference electrode and the potential difference between the reference and working electrodes, the potential of the working electrode can be inferred and circuitry used to control it as the desired level. This knowledge and control of working electrode potential is essential in Daruházi because the relationship of the current to the potential of the working electrode is what is required in the cyclic voltammetry method.
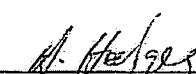
26.   Diebold and White, on the other hand, cannot perform the cyclic voltammetry method as designed because they only include two electrodes and do not contain the necessary electronics. It is not possible to know the potential of the working electrodes of Diebold and White with any accuracy because the respective counter electrode does not have a known reference potential. Further, if only a reference electrode and working electrode are used, then either the mediator in the solution (e.g., ferricyanide) will interfere with the potential of the reference electrode in an unknown way, thereby again not allowing for a measurement of the potential of the working electrode, or the mediator would not react appreciably at the reference electrode, in which case the electrochemical conditions required for the teachings of Daruházi to work would not be present. It is a condition for the teachings of Daruházi to work that the redox species be regenerated at the auxiliary electrode to establish a steady-state current. (*See at least* Abstract on p. 77.) If the mediator does not react appreciably at a reference electrode, as would be the case if the counter/reference electrode used with the teachings of Diebold and White acted as a source of an accurately known reference potential, then the redox species would not be regenerated and thus the teachings of Daruházi would fail. It is thus clear that the two electrode systems of Diebold and White could not function in the way required

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for the teachings of Daruházi to be successful with the configurations of Diebold and White.

27.   The methods taught by Daruházi are further not desirable because of the inaccurate results produced by its teachings. Not only would the results of Daruházi be inaccurate if incorporated with the devices of Diebold and White because the results are non-Cottrell, but the results independent of the devices with which the teachings are combined are also inaccurate. Daruházi explains as much in paragraph 5 on page 87. Because Daruházi relies on I_{max}, a background current correction is necessary. (*See* p. 87, para. 5.) The result of the calculations leads to a scatter in the values of the Diffusion coefficient (D) and the distance between the working electrode and the auxiliary electrode (δ). According to Daruházi, the scatter is a result of the deficiencies in the slow potential sweep method, and specifically is attributed to: "(i) some errors in the evaluation of I_{max} due to the correction of the background current, (ii) relatively large uncertainty in p determined from I_{max}/I_{ss} value close to unity, (iii) any effect of the products generated at the auxiliary electrode from the reaction of the supporting electrolyte or water, and/or (iv) any change in the electrode surface activity under the same clamping conditions of the cell to keep d constant during a series of experiments." A person having ordinary skill in the art, in view of these deficiencies, would not be inclined to incorporate these inaccurate techniques into a device like Diebold and/or White.

28.   I further declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issuing thereon.

Date: JULY 2, 2009

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Alastair Hodges

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